Latest SIRT recommendations from EU proctors

*Geert Maleux**

University Hospitals Leuven, Belgium

***Address for correspondence:** Geert Maleux MD, PhD, Department of Radiology, University Hospitals Leuven, Herestraat 49, B3000 Leuven, Belgium

1.Introduction to the training, evaluation and certification programme

Proctors are suitably qualified physicians or clinicians, mostly interventional radiologists with extensive experience in selective internal radiation therapy (SIRT) using yttrium-90 (^{90}Y) resin microspheres (SIR-Spheres microspheres, Sirtex Medical Ltd, Sydney, Australia), who have been contracted to act as trainers on behalf of Sirtex.

The Training, Evaluation and Certification programme is consistent with the US Nuclear Regulatory Commission (NRC) guidelines that require a new authorised user to attend three training sessions delivered by either a Sirtex representative or trained physician proctor. After three procedures, the proctor reviews the centre's procedures to confirm that SIRT is being safely and effectively delivered since the outcome for patients is almost wholly determined by the skill of the interventional radiologist in performing this procedure.

For the first SIRT procedure, the institute is required to send pre-treatment patient data to the proctor at least 5 days before the treatment date including: the patient‘s history on prior chemotherapy /biological therapy, prior abdominal surgery, functional status and physical examination data (blood test results, imaging results, mapping arteriograms, technetium-99m macroaggregated albumin [^{99m}*Tc-MAA*] lung shunt study results and intended treatment plan). In accordance with established guidelines from the peer-reviewed medical literature, it is important that the interventional radiologist

who performs the SIRT procedure also performs the baseline mapping angiogram, thereby ensuring continuity of patient care and better training.

2. Recommended procedures for generating mapping angiograms

When CT angiography is available it should be reviewed prior to undertaking the mapping angiography to assist in detecting anatomy and the need for selective angiography (including the superior mesenteric artery and celiac axis) [1]. The mapping procedures should be conducted using an automated pump injection in order to identify not only the right and left hepatic arteries, but also the gastric arteries and any other accessory vessels, which may need to be coil embolised to ensure the safe administration of ^{90}Y-resin microspheres. Suggested arterial contrast injection rates and volumes (Table 1) should be individualised according to the patient and vessel caliber with filming carried out into the late venous phase. When injecting approximately 4 mCi of ^{99m}Tc-MAA, the catheter tip must be positioned in the same place as intended for the injection of the ^{90}Y-resin microspheres. Within one hour of the ^{99m}Tc-MAA injection, planar scintigraphic imaging should be performed with regions of interest drawn around the lungs and the liver and the counts for each region measured [2]. Early scintigraphic imaging is essential for ensuring the accurate assessment of lung shunting (since shunt fractions that could result in > 25Gylung radiation dose may exclude the patient from SIRT treatment). Importantly, the ^{99m}Tc-MAA study should be performed within 4 weeks prior to the planned SIRT treatment date and generally not on the same day as the SIRT procedure. Combining ^{90}Y-resin microspheres and ^{99m}TC-MAA, may however be feasible in appropriately selected patients. For example, investigators from the University Hospital Bonn combined ^{90}Y-resin microspheres with a simultaneous second test angiogram of another lobe or segments in the same session in six patients [3]. In this study, immediate post-therapeutic ^{99m} Tc-MAA SPECT/CT showed only the distribution of ^{99m}Tc-MAA without any detectable ^{90}Y-Bremsstrahlung SPECT/CT; while a post-therapeutic Bremsstrahlung SPECT/CT scan conducted 48 hours later could be performed without any ^{99m}Tc-MAA contamination.

It is clear from the experience of the Nuclear Medicine Physicians from University Hospital Bonn that SPECT/CT has much higher sensitivity and specificity than planar or non-attenuation-corrected SPECT for the assessment of extrahepatic MAA deposition [4]. In pre-SIRT planning, ^{99m}Tc-MAA SPECT/CT is the most valuable technique for identifying extrahepatic visceral sites at risk for post-SIRT complications. In these patients, further coil embolisation may be necessary; alternatively the catheter can be placed distal to the extrahepatic artery in order to ensure the safe delivery of SIRT (Figure 1). For the cystic arteries, however, coil embolisation is not considered necessary because the respective risks of ischaemic injury or radiation injury to the gallbladder are similar with and without embolisation (~5%).

3. Predictive value of intratumoral ^{99m}Tc-macroaggregated albumin uptake

Response to SIRT was found to be independent of the degree of ^{99m}Tc-MAA uptake [5]. Therefore, it is the view of the proctors that SIRT should not be withheld from patients with colorectal liver metastases lacking intratumoral ^{99m}Tc-MAA accumulation.

4. D**osimetry**

The calculation of the activity to be delivered should be discussed by the radiologist and the nuclear medicine physician during the multidisciplinary team meeting. Some important practice points to consider are as follows:

- The point of injection (tip of the catheter position) and the activity delivered must be marked on the scans for follow-up
- Body surface area (BSA) model is the preferred method of calculation of the prescribed activity
- Tumour volume should be calculated (not estimated) from CT
- Consider reduction in prescribed activity by 20-30% for the following patients:

- Heavily pre-treated
- Cirrhotics
- 5-10% tumour burden (high tumour burden : case dependent)
- Small livers (<1200-1500 cc)[6]

These recommendations are based on recent study from the Pamplona group [6] who showed that the incidence of Radioembolisation (SIRT) Induced Liver Disease (REILD) was reduced by lowering the treatment intensity in patients who had received prior exposure to cancer chemotherapy, cirrhosis or a reduced liver and/or tumour volume. By contrast, treatment intensity could be safely increased with more selective SIRT with a radical intent. In all patients, 600 mg/d of ursodeoxicolic acid was given for 2 months post-SIRT [6].

5. Peri-procedural care

The following recommendations [7] have been published:

- Proton Pump Inhibitor (PPI) must be given *at least* for 1 week after SIRT
    - *better:* starting 1 week before and given for 4 weeks after SIRT
- Pain medication is should be given either before or during the SIRT procedure
- Corticosteroids may be given 24 hours before and for a minimum of 1 week after the treatment
    - or better: 8 mg qd for 4 weeks and 4 mg qd for another 4 weeks
- Anti-emetics are usually commenced on the morning of the day of SIRT treatment
- Antibiotics are not recommended unless the patient has had biliary surgery, prior stent implantation or a bile duct obstruction
- Carcinoid crisis prophylaxis: short-acting somatostatin analogue should be considered for the prevention of carcinoid crisis
- 2x-300 mg Ursodeoxycholicacid for (4-) 8 weeks

In addition, administration of 300 mg sodium perchlorate (NaCl04)(20-30 gtt) min. 2 – 4 hours before application of ^{99m}Tc-MAA is recommended in order to inhibit the Na-I-symporter protein in the gastric mucosa, thereby making it easier to discriminate between gastric / extrahepatic MAA and gastric accumulation of free pertechnetate [8].

6. General principles for repeated SIRT

The following general principles should be applied when considering repeat SIRT [7]:

- Time interval from 1st or most recent ^{90}Y treatment should be at least 12 weeks (taking into account the typical tumour response by RECIST or WHO between 10-14 weeks post SIRT)
- A more selective treatment strategy should be considered so segments of the liver can be spared radiation during subsequent treatment
- Interval therapies since last SIRT can impact on liver tolerance and may lead to either a reduced activity planned or avoidance of a lobe or segment for retreatment.
- Trends in functional liver reserve parameters (AP, GOT, GPT, bilirubin, albumin) over past 3 months are helpful

7. The Coldwell "Sandwich" delivery technique

Today, it is recommended that ^{90}Y-resin microspheres are injected using the Coldwell "Sandwich" Delivery Technique which involves putting the aliquot of ^{90}Y-resin microspheres into the line first followed by 1 mL of sterile water then 1-2 mL of contrast (full strength). While using fluoroscopy, the entire content should be pulsed through the microcatheter using a 20 mL syringe constantly so that the pulsing creates a turbulent flow for the more even delivery of the the microspheres. Once the contrast is observed (indicating that the microspheres have been delivered), the pressure on the sterile water syringe can be increased to check the flow in the treated artery.

The advantage of this technique is that: the catheter tip is watched continuously so that it does not inadvertently move into another artery; the flow is seen at each injection and so there is no need to do a true arteriogram that wastes contrast and time; and finally, the delivery is safer since the operator knows immediately when the flow slows down.

References

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Table 1. Suggested Arterial rates and volumes recommended for generating mapping angiograms

Vessel	Injection Rate	Volume	Acquisition
SMA			
Celiac axis	5-7cc/sec	20-30cc	2-3fps/12s-1fps/20s
Proper HA	4cc/sec	12cc	2-3fps/10s-1fps/20s
Replaced HA	2-4cc/sec	8-16cc	2-3fps/10s-1fps/20s
Right or left HA	1-3cc/sec	4-12cc	2-3fps/10s-1fps/20s

Liu D et al. J Vasc Interv Radiol 2005;16:911-935

Figure 1. Procedure for identifying extrahepatic visceral sites at risk for post-SIRT complications